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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,843	09/28/2006	Mariusz W. Szkudlinski	TROP-002/01US 304828-2049	3706

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EXAMINER	
RIDER, LANCE W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,843	SZKUDLINSKI ET AL.	
	Examiner	Art Unit	
	LANCE RIDER	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-50 and 76-80* is/are pending in the application.

4a) Of the above claim(s) *29,31-36 and 40-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30,37-39,50 and 76-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 28-50 and 76-80 are currently pending, claims 29, 31-36, 40-49 have been withdrawn due to the election requirement filed on June 10th 2010.

Election/Restrictions

Applicant's election without traverse of Group II, claims 28-50 and 76-80 in the reply filed on June 10th 2010 is acknowledged.

Applicant's election of the species of follicle stimulating hormone with substitutions of Q13R, E14R, P16R, and Q20R, doxorubin, and ovarian cancer in the reply filed on June 10th 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 28, 30, 37-39, 50, and 76-80 read on the instantly elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28, 30, 37-39, 50, and 76-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s)

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has elected the instant species of follicle stimulating hormone with substitutions of Q13R, E14R, P16R, and Q20R, and doxorubin. Neither the specific species of follicle stimulating hormone with substitutions of Q13R, E14R, P16R, and Q20R, nor the species of doxorubin are found in the specification of the original set of claims. For doxorubin the examiner is interpreting "doxorubin" to be a misspelling of doxorubicin. As to the specific species of follicle stimulating hormone, applicant has described a Markush of follicle stimulating hormones surrounding the species elected but has no claim or embodiment of the instantly elected species in either the original filed specification or claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28, 30, 37-39, 50, and 76-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 recites the phrase "a modified glycoprotein hormone having at least one mutation that increases the hormone activity relative to the wild type glycoprotein hormone". What is a modified glycoprotein hormone? The present specification provides no sequences nor any indication of the specific species and isoform of wild type follicle

stimulating hormone which is modified. As there is no indication of the starting sequence it is impossible to identify the sequence being claimed, rendering the claim indefinite. Furthermore what is a "mutation that increases the hormone activity relative to wild type"? Is the increase in activity an increase in bioavailability? Is it an increase in binding, or an increased activation of the hormones target? This phrase renders the claim indefinite. Claims 30, 37-39, 50, and 76-80 depend upon this independent claim and do not rectify its indefinite nature.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 30, 37-39, 50, and 76-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nett et al., U.S. Patent Application Publication 2002/0165126 in view of Williams et al., U.S. Patent 5,703,039 and Szkudlinski, M.W., et al., U.S. Patent 6,361,992.

Nett teaches methods of treating patients in need of treatment by administering follicle stimulating hormone conjugated to doxorubicin to them. (See claims 1 and 2 of Nett.) Nett also teaches that such compounds can be used to treat sex hormone related cancers. (See paragraph 0056.)

Nett does not teach the use of follicle stimulating hormone conjugated to a toxin to treat ovarian cancer.

Williams teaches methods to treat hormone related cancers (melanocytes) with follicle stimulating hormone conjugated to a toxin, and states that follicle stimulating hormone is specific for ovarian cells. (See column 15 line 55 trough column 6 line 16.)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use the known doxorubicin(toxin)-follicle stimulating hormone conjugate used to treat cancers as described by Nett in a cancer treatment for ovarian

cancer using follicle stimulating hormone conjugated to a toxin as described by Williams in order to form an equivalent method of treating ovarian cancer. The skilled artisan would have expected that this combination would function as Williams expressly teaches that follicle stimulating hormone is specific for ovarian cells and toxin-hormone conjugates can be used to treat cancers of such tissues. Nett provides just such a toxin-hormone conjugate which can be used to treat cancers.

Nett and Williams do not teach using a follicle stimulating hormone with enhanced binding activity in their conjugates.

Szkudlinski teaches modified human glycoprotein hormones such as follicle stimulating hormone modified in the alpha subunit to contain at least 3 basic amino acids at positions 13, 14, 16, and 20, wherein the basic amino acids are either lysine or arginine. (See column 11, lines 1-67.) Szkudlinski teaches that these modifications increase the binding of the hormone to the target cells and increases their activity. This means less hormone is needed to target or activate the cells. (See column 2, lines 1-27 and table II.)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to substitute the modified follicle stimulating hormones of Szkudlinski for the follicle stimulating hormones of Nett and Williams in order to form a more active tighter binding toxin-follicile stimulating hormone conjugate in order to provide a more active drug to ovarian cancer patients. The skilled artisan would have expected that this combination would function as Nett and Williams teach using follicle stimulating hormone conjugates to treat ovarian cancer and Szkudlinski teaches just

such a follicle stimulating hormone. This modified follicle stimulating hormone binds to its target more tightly, which would still allow it to target the ovarian cells, just more selectively and with less active conjugate needed to target those cells.

Conclusion

No claims are currently allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/
Examiner, Art Unit 1618

/Jake M. Vu/
Primary Examiner, Art Unit 1618